

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

Amendments to the Claims:Claim 1 (withdrawn):

An array for screening to identify conditions, compounds, or compositions that inhibit, prevent, induce, modify, or reverse transitions of physical state comprising at least 24 samples, each sample comprising a medium, wherein one or more of the samples comprises a disease-causing substance.

Claims 2-14 (canceled).Claim 15 (withdrawn):

A method of preparing an array of at least 24 samples for screening to identify conditions, compounds, or compositions that inhibit, prevent, induce, modify, or reverse transitions of physical state comprising: (a) adding a medium to each of the samples; and (b) adding a disease-causing substance to at least one of the samples.

Claims 16-50 (canceled).Claim 51 (withdrawn):

A method to discover conditions, compounds, or compositions that prevent or inhibit crystallization, precipitation, polymerization, or deposition of a disease-causing substance, or promote depolymerization comprising: (a) preparing an array comprising at least 24 samples each sample comprising a medium and one or more components to induce a disease-causing substance; (b) processing one or more of the samples to induce crystallization, precipitation, or deposition of the disease-causing substance; (c) screening the array by analyzing the processed samples to detect the absence of crystallization, precipitation, polymerization, depolymerization, or deposition of the disease-causing substance; and (d) selecting the samples wherein crystallization, precipitation, polymerization, depolymerization, or deposition of the disease-causing substance did not occur to identify the conditions, compounds, or compositions.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/chm

Claims 52-65 (canceled).Claim 66 (withdrawn):

A method to discover conditions, compounds or compositions that promote dissolution, destruction, or breakup of a disease-causing substance, comprising: (a) preparing an array comprising at least 24 samples each sample comprising a medium and the disease-causing substance; (b) processing one or more of the samples to induce the dissolution, destruction, or breakup of the disease-causing substance; (c) screening the array by analyzing the processed samples to detect the dissolution, destruction, depolymerization, or breakup of the disease-causing substance; and (d) selecting the samples wherein the dissolution, destruction, depolymerization, or breakup of the disease-causing substance occurred to identify the conditions, compounds, or compositions.

Claims 67-80 (canceled).Claim 81 (new):

A method of screening an array of at least 96 samples to identify conditions, compounds, or compositions that inhibit or prevent transitions of physical state comprising:

- (a) preparing and identifying an array of at least 96 samples in tubes and support plates or in sample well plates and dispensing a medium, a disease-causing substance in liquid or dissolved form and one or more additional components into sample tubes or sample wells with an automated distribution mechanism, and each sample differs with respect to at least one of:
 - the amount or concentration of the disease-causing substance;
 - an identity of one or more of the additional components; or
 - an amount or concentration of one or more of the additional components;
- (b) processing one or more of the samples to induce crystallization, precipitation or deposition of the disease causing substance;

5

Docket No. TPI-T600XC1
Serial No. 09/994,585

- (c) analyzing the processed samples to detect the induction of said crystallization, precipitation or deposition; and
- (d) selecting those processed samples that exhibit inhibition or prevention of a transition in physical state.

Claim 83 (new):

The method of claim 81, comprising dispensing said disease-causing substance in dissolved form.

Claim 84 (new):

The method of claim 81, comprising dispensing said disease-causing substance in liquid form.

Claim 85 (new):

The method of claim 81, wherein said processing comprises heating said samples in a sample incubation module to a temperature (T1), analyzing said samples for the presence of undissolved solids using visual analysis, and cooling said samples to a final temperature (T2).

Claim 86 (new):

The method of claim 81, comprising the addition of said samples to tubes in a support plate.

Claim 87 (new):

The method of claim 86, wherein said tubes are glass tubes and said support plate is a metal support plate.

Claim 88 (new):

The method of claim 86, comprising sealing said tubes with a cap.

J:\TPI-T600XC1\PTO\resp2d.doc/DNB/ehm

6

Docket No. TPI-T600XC1

Serial No. 09/994,585

Claim 89 (new):

The method of claim 88, wherein said cap is pierced with a standard syringe needle and fluid aspirated through the syringe tip to remove solvent from the sample.

Claim 90 (new):

The method of claim 81, wherein said array comprises at least 1000 samples.

Claim 91 (new):

The method of claim 81, further comprising the generation of a work list for instructing an automated distribution mechanism to prepare said array of samples.

Claim 92 (new):

The method of claim 81, wherein said sample contains less than 1 milligram of said disease-causing substance.

Claim 93 (new):

The method of claim 88, comprising the piercing of said cap and aspiration of medium from said samples.

Claim 94 (new):

The method of claim 81, comprising analyzing said array of samples with a polarized light filter apparatus.

Claim 95 (new):

The method of claim 81, wherein the additional component is a small molecule.

Claim 96 (new):

The method of claim 81, wherein said array comprises at least 1 sub-array.

J:\TPI-T600XC1\PTO\rcsp2d.doc/DNB/ehm

7

Docket No. TPI-T600XC1
Serial No. 09/994,585Claim 97 (new):

The method of claim 81, wherein said array comprises at least 1 sub-array with at least 24 samples.

Claim 98 (new):

The method of claim 81, wherein said processing comprises adjusting a time of incubation.

Claim 99 (new):

The method of claim 81, wherein said processing comprises adjusting a temperature.

Claim 100 (new):

The method of claim 81, wherein said processing comprises adjusting a pressure.

Claim 101 (new):

The method of claim 81, wherein said processing comprises subjecting the samples to a nucleation event.

Claim 102 (new):

The method of claim 81, wherein said processing comprises subjecting the samples to ultrasound, shock waves, laser energy, or mechanical stimulation.

Claim 103 (new):

The method of claim 81, wherein said processing comprises adjusting an amount of a component.

Claim 104 (new):

The method of claim 81, wherein said processing comprises adding a component.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/chm

Claim 105 (new):

The method of claim 81, wherein said processing comprises adjusting an amount of the medium.

Claim 106 (new):

The method of claim 81, wherein said processing comprises adjusting a gas composition.

Claim 107 (new):

The method of claim 81, wherein the disease-causing substance is calcium phosphate, calcium carbonate, calcium pyrophosphate, brushite, apatite, hydroxyapatite, calcium oxalate, a kidney stone, bone tissue, magnesium ammonium phosphate, uric acid, a salt of uric acid, a gall stone, cholesterol, an amyloid protein, collagen, bilirubin, a salt of bilirubin, dental plaque, dental calculus, protein structure, a protein precipitate, a hydrate thereof or a mixture thereof.

Claim 108 (new):

The method of claim 81, wherein the processed samples are analyzed to detect a solid or an absence of a solid.

Claim 109 (new):

The method of claim 108, wherein a detected solid is analyzed to determine if the solid is amorphous or crystalline.

Claim 110 (new):

The method of claim 81, wherein at least about 100 samples are screened per day.

Claim 111 (new):

The method of claim 107, wherein at least about 1000 samples are screened per day.

Claim 112 (new):

The method of claim 81, wherein an individual sample within said array is subjected to processing methods that are different from the processing methods to which another sample is subjected.

Claim 113 (new):

The method of claim 112, wherein said individual sample is subjected to processing methods comprising introducing a nucleation event.

Claim 114 (new):

The method of claim 112, wherein said individual sample is subjected to processing methods comprising adding one or more additional components.

Claim 115 (new):

The method of claim 81, wherein said array comprises sub-arrays, and wherein an individual sample within a sub-array is subjected to processing methods that are different from the processing methods to which another sample within the sub-array is subjected.

Claim 116 (new):

The method of claim 115, wherein said individual sample is subjected to processing methods comprising introducing a nucleation event.

Claim 117 (new):

The method of claim 115, wherein said individual sample is subjected to processing methods comprising adding one or more additional components.

10

Docket No. TPI-T600XC1
Serial No. 09/994,585Claim 118 (new):

The method of claim 81, wherein said array comprises sub-arrays, and wherein an individual sub-array is subjected to processing methods that are different from the processing methods to which another sub-array is subjected.

Claim 119 (new):

The method of claim 118, wherein said individual sub-array is subjected to processing methods comprising introducing a nucleation event.

Claim 120 (new):

The method of claim 118, wherein said individual sub-array is subjected to processing methods comprising adding one or more additional components.

Claim 121 (new):

The method of claim 81, wherein said disease-causing substance has a molecular weight less than about 1000 g/mol.

Claim 122 (new):

The method of claim 81, wherein the amount of said disease-causing substance in each sample is less than about 1 milligram.

Claim 123 (new):

The method of claim 81, wherein the amount of said disease-causing substance in each sample is less than about 100 micrograms.

Claim 124 (new):

The method of claim 81, wherein the amount of said disease-causing substance in each sample is less than about 100 nanograms.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/ehm

11

Docket No. TPI-T600XC1
Serial No. 09/994,585Claim 125 (new):

The method of claim 81, wherein each sample has a total volume between 5-500 μ l.

Claim 126 (new):

The method of claim 81, wherein each sample has a total volume between 10-200 μ l.

Claim 127 (new):

The method of claim 81, wherein one or more samples differ from one or more other samples with respect to the amount of the disease-causing substance.

Claim 128 (new):

The method of claim 81, wherein one or more samples differ from one or more other samples with respect to the amount of the medium.

Claim 129 (new):

The method of claim 81, wherein one or more samples differ from one or more other samples with respect to the amount of the identity or the amount of the components.

Claim 130 (new):

The method of claim 81, wherein crystal nucleation and growth is controlled by the concentration of components.

Claim 131 (new):

The method of claim 81, wherein crystal nucleation and growth is controlled by the identities of components.

Claim 132 (new):

The method of claim 81, wherein crystal nucleation and growth is controlled by temperature.

J:\TPI\T600XC1\PTO\resp2d.doc\DNB/ehm

12

Docket No. TPI-T600XC1
Serial No. 09/994,585Claim 133 (new):

The method of claim 81, wherein said analyzing is by machine vision technology.

Claim 134 (new):

The method of claim 81, wherein said analyzing is by video-optical microscopy.

Claim 135 (new):

The method of claim 81, wherein said analyzing is by image analysis.

Claim 136 (new):

The method of claim 81, wherein said analyzing is by polarized light analysis.

Claim 137 (new):

The method of claim 81, wherein said analyzing is by near field scanning optical microscopy.

Claim 138 (new):

The method of claim 81, wherein said analyzing is by far field scanning optical microscopy.

Claim 139 (new):

The method of claim 81, wherein said analyzing is by atomic-force microscopy.

Claim 140 (new):

The method of claim 81, wherein said analyzing is by micro-thermal analysis.

Claim 141 (new):

The method of claim 81, wherein said analyzing is by infrared spectroscopy.

J:\TPI\T600XC1\PTO\resp2d.doc/DNB/ehm

13

Docket No. TPI-T600XC1
Serial No. 09/994,585Claim 142 (new):

The method of claim 81, wherein said analyzing is by near infrared spectroscopy.

Claim 143 (new):

The method of claim 81, wherein said analyzing is by Raman spectroscopy.

Claim 144 (new):

The method of claim 81, wherein said analyzing is by NMR.

Claim 145 (new):

The method of claim 81, wherein said analyzing is by x-ray diffraction.

Claim 146 (new):

The method of claim 81, wherein said analyzing is by neutron diffraction.

Claim 147 (new):

The method of claim 81, wherein said analyzing is by powder x-ray diffraction.

Claim 148 (new):

The method of claim 81, wherein said analyzing is by light microscopy.

Claim 149 (new):

The method of claim 81, wherein said analyzing is by second harmonic generation.

Claim 150 (new):

The method of claim 81, wherein said analyzing is by electron microscopy.

Claim 151 (new):

The method of claim 81, wherein said analyzing is by an *in vitro* assay.

J:\TPI-T600XC1\PTO\resp2d.doc/DNB/ehm